Hypogonadism in females with Prader-Willi syndrome from infancy to adulthood: variable combinations of a primary gonadal defect and hypothalamic dysfunction

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Objective: The variable hypogonadism in Prader-Willi Syndrome (PWS) has generally been attributed to hypothalamic dysfunction. Recent studies documented primary testicular dysfunction in PWS males. Our aims were to characterize sexual development and reproductive hormones in PWS females and to investigate the etiology of hypogonadism.

Design: a cross-sectional study.

Methods: Physical examination was performed on 45 PWS females (ages 6 weeks to 32 years) and blood samples were obtained for hormonal analyses.

Results: Age of onset and progression of puberty varied; most adults had incomplete sexual development. Spontaneous menarche was reported in 4 (ages 15-30 years) but all had subsequently developed secondary amenorrhea or oligomenorrhea. Anti-Mullerian hormone levels were within the normal range in all age groups. Inhibin B was consistently low or undetectable; only 5 women had levels in the low-normal range (20-54 pg/mL). LH was normal in most children but low (<1.0 IU/L) in 9 of 15 adults. FSH was within the normal range for age in most, but low (<0.5 IU/L) in 10 and high in 4. Estradiol levels were normal-low and androgen levels were normal in the majority.

Conclusions: Pubertal development in PWS females, as in males, is characterized by normal adrenarche, pubertal arrest and hypogonadism due to variable combinations of a unique primary gonadal defect and hypothalamic dysfunction.